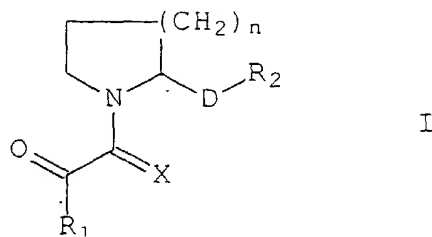


What is claimed is:

1. A compound having the formula (I):



5 where

n is 1-3;

X is either O or S;

R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is a carboxylic acid or a carboxylic acid isostere; and wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup> and Z, where

R<sup>3</sup> and Z are independently hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, or CO<sub>2</sub>R<sup>7</sup> where R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl;

or a pharmaceutically acceptable salt, ester, or solvate

thereof;

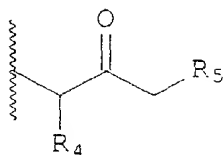
provided that:

when  $n=1$ , and D is a bond, and  $R_2$  is COOH,

then  $R_1$  is not  $C_1-C_9$  straight or branched chain alkyl,  $C_2-C_9$  straight or branched chain alkenyl,  $C_5-C_7$  cycloalkyl,  $C_5-C_7$  cycloalkenyl, phenylamine, 2-(3,4-dichlorophenyl)ethyl, hydroxy, ethoxy, benzyl, or  $Ar_1$ , where  $Ar_1$  is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 1-pyridyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, and wherein said alkyl, alkenyl, cycloalkyl, cycloalkenyl, or  $Ar_1$  are optionally substituted with one or more substituents selected from the group consisting of hydrogen, halo, hydroxyl, nitro, trifluoromethyl,  $C_1-C_9$  straight or branched alkyl,  $C_2-C_9$  straight or branched alkenyl,  $C_1-C_4$  alkoxy,  $C_2-C_4$  alkenyloxy, phenoxy, benzyloxy, COOH, and amino;

further provided that:

when  $n=1$ , and D is a bond, and  $R_2$  is the carboxylic acid isostere  $-CONZ(R^3)$ , and Z is hydrogen or  $C_1-C_6$  alkyl, and  $R^3$  is phenyl, or  $C_2-C_6$  straight or branched chain alkyl or alkenyl, wherein said alkyl is unsubstituted or substituted in one or more positions with  $Ar_2$  as defined below,  $C_3-C_9$  cycloalkyl, cycloalkyl connected by methyl or a  $C_2-C_6$  straight or branched chain alkyl or alkenyl chain,  $C_1-C_4$  alkyl ester, or  $Ar_3$  where  $Ar_3$  is selected from the group consisting of 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl,  $C_1-C_6$  straight or branched alkyl,  $C_2-C_6$  straight or branched alkenyl,  $C_1-C_4$  alkoxy,  $C_2-C_4$  alkenyloxy, phenoxy, benzyloxy, and amino; wherein said alkyl ester is optionally substituted with phenyl; or  $R^3$  is the fragment:



where  $R_4$  is selected from the group consisting of straight or branched chain  $C_1-C_8$  alkyl optionally substituted with  $C_3-C_8$  cycloalkyl, benzyl, or  $Ar_2$  as defined below, and where  $R_2$  is  
 5  $COOZ$  or  $CONR^6$ , where  $R^6$  is selected from the group consisting of hydrogen,  $C_1-C_6$  straight or branched alkyl, and  $C_2-C_6$  straight or branched alkenyl, and where  $R_5$  is selected from the group consisting of phenyl, benzyl,  $C_1-C_6$  straight or  
 10 branched alkyl, and  $C_2-C_6$  straight or branched alkenyl, where said alkyl or alkenyl is optionally substituted with phenyl; then  $R_1$  is not  $C_1-C_8$  straight or branched chain alkyl,  $C_2-C_8$  straight or branched chain alkenyl, substituted thiophene, or  $C_1-C_2$  alkoxy, wherein said alkyl or alkenyl is optionally  
 15 substituted in one or more positions with  $C_3-C_8$  cycloalkyl,  $C_5-C_7$  cycloalkenyl, or  $Ar_2$ , where  $Ar_2$  is defined below, where said alkyl, alkenyl, cycloalkyl or cycloalkenyl groups may be optionally substituted with  $C_1-C_4$  alkyl,  $C_1-C_4$  alkenyl, or hydroxy, and where  $Ar_2$  is 1-naphthyl, 2-naphthyl, 2-indolyl,  
 20 3-indolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl,  $C_1-C_6$  straight or branched alkyl,  $C_2-C_6$  straight or branched alkenyl,  $C_1-C_4$   
 25 alkoxy,  $C_2-C_4$  alkenyloxy, phenoxy, benzyloxy, and amino; further provided that:  
 when  $n=1$ , and  $X$  is  $O$ , and  $D$  is a bond, and  $R_2$  is  $-CONH_2$ , then  $R_1$  is not methyl, ethyl, iso-propyl, iso-butyl, iso-pentyl, 4-methylpentyl, indolyl, phenyl, or hydroxyphenyl;  
 30 further provided that:

when  $n=1$ , and X is O, and D is a bond, and  $R_2$  is cyano, then  $R_1$  is not methyl;

further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $\text{CONZ}(R^3)$ ,  
5 and  $R_1$  is ethoxy, then  $R^3$  or Z is not halo-substituted phenyl;

further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $\text{CONZ}(R^3)$  and  
 $R_1$  is substituted thiophene or tetrahydropyranoxy, or  
10 methoxy, then  $R^3$  or Z is not  $C_1$ - $C_4$  alkyl ester substituted ethyl;

further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $\text{CONZ}(R^3)$  and  
 $R_1$  is ethoxy, then  $R^3$  or Z is not 4-chlorophenyl;

15 further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is  $\text{CONZ}(R^3)$  and  
 $R_1$  is cyclohexyl, then  $R^3$  or Z is not ethyl or propyl  
substituted with phenyl;

further provided that:

20 when D is  $\text{CH}_2$ , then  $R_2$  is not -OMe, -NHMe, or substituted  
-NHcyclohexyl;

further provided that:

when D is  $\text{CH}_2$ , and  $R_2$  is -OH,  
then  $R_1$  is not phenyl or pyrrolidinemethanol;

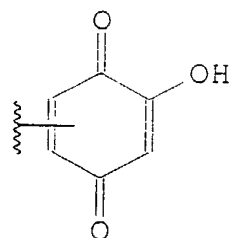
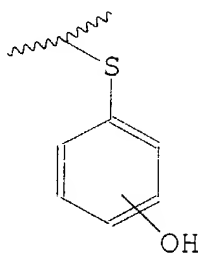
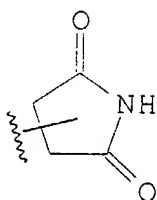
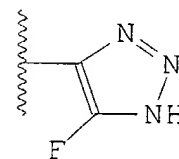
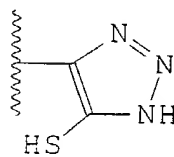
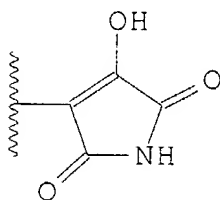
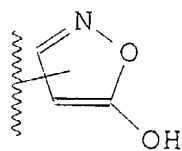
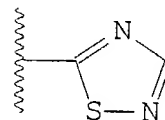
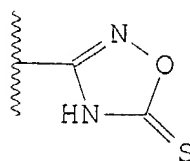
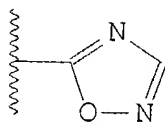
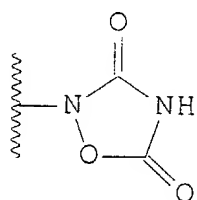
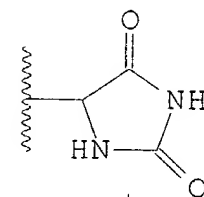
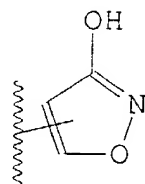
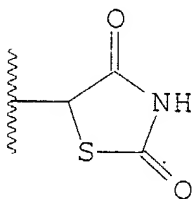
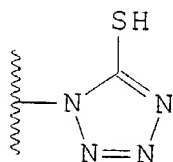
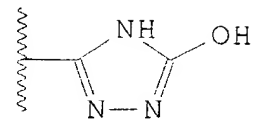
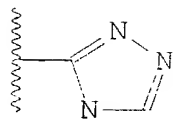
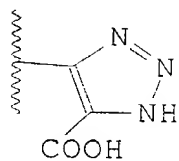
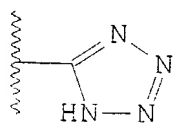
25 further provided that:

when  $n=2$ , and X is O, and D is a bond, and  $R_2$  is COOH,  
then  $R_1$  is not methyl, tert-butyl, 1,1-dimethyl-2-methyl-  
propyl, 1,1-dimethyl-propyl, methoxy, ethoxy, phenyl,  
tetrahydropyranoxy substituted  $C_4$ - $C_6$  alkyl, 1-methyl-1-  
30 methoxyamide, 1-methylcyclohexyl, 3-iodophenyl, 3-methyl  
ester-cyclopentyl, 1,1-dimethyl-6-phenyl-hex-3,5-dioxy, or  
trimethoxyphenyl.

2. The compound of claim 1, wherein  $R_2$  is a carbocycle or  
35 heterocycle containing any combination of  $\text{CH}_2$ , O, S, or N in

any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R<sup>3</sup>.

- 5     3.     The compound of claim 1, wherein R<sub>2</sub> is selected from the group consisting of:



where the atoms of said ring structure may be optionally substituted at one or more positions with R<sup>3</sup>.

4. The compound of claim 1, wherein R<sub>2</sub> is selected from the group consisting of:

-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>; -NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CONZ(R<sup>3</sup>); -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>; -COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

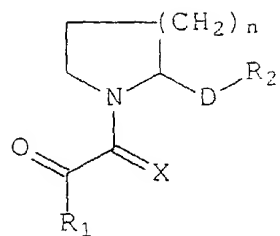
5. The compounds, (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinetetrazole; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarbonitrile; and (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-aminocarbonyl piperidine; and compounds 1-25, 27, 28, 31-33, and 35-136 of Tables I, II, and III.

6. The compound 1-{2-[3-(4-Fluorophenyl)(1,2,4-oxadiazol-5-yl)]pyrrolidinyl}-3,3-di-methylpentane-1,2-dione.

7. The compound 3,3-Dimehyl-1-[2-(3-methyl(1,2,4-oxadiazol-5-yl))pyrrolidinyl]pentane-1,2-dione.

8. A pharmaceutical composition, comprising:  
a) an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere; and  
b) a pharmaceutically acceptable carrier.

9. The pharmaceutical composition of claim 8, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



where

n is 1-3;

X is either O or S;

5 R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

10 D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>1</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere;

and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

15 R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> where  
20 R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl;  
or a pharmaceutically acceptable salt, ester, or solvate  
25 thereof.

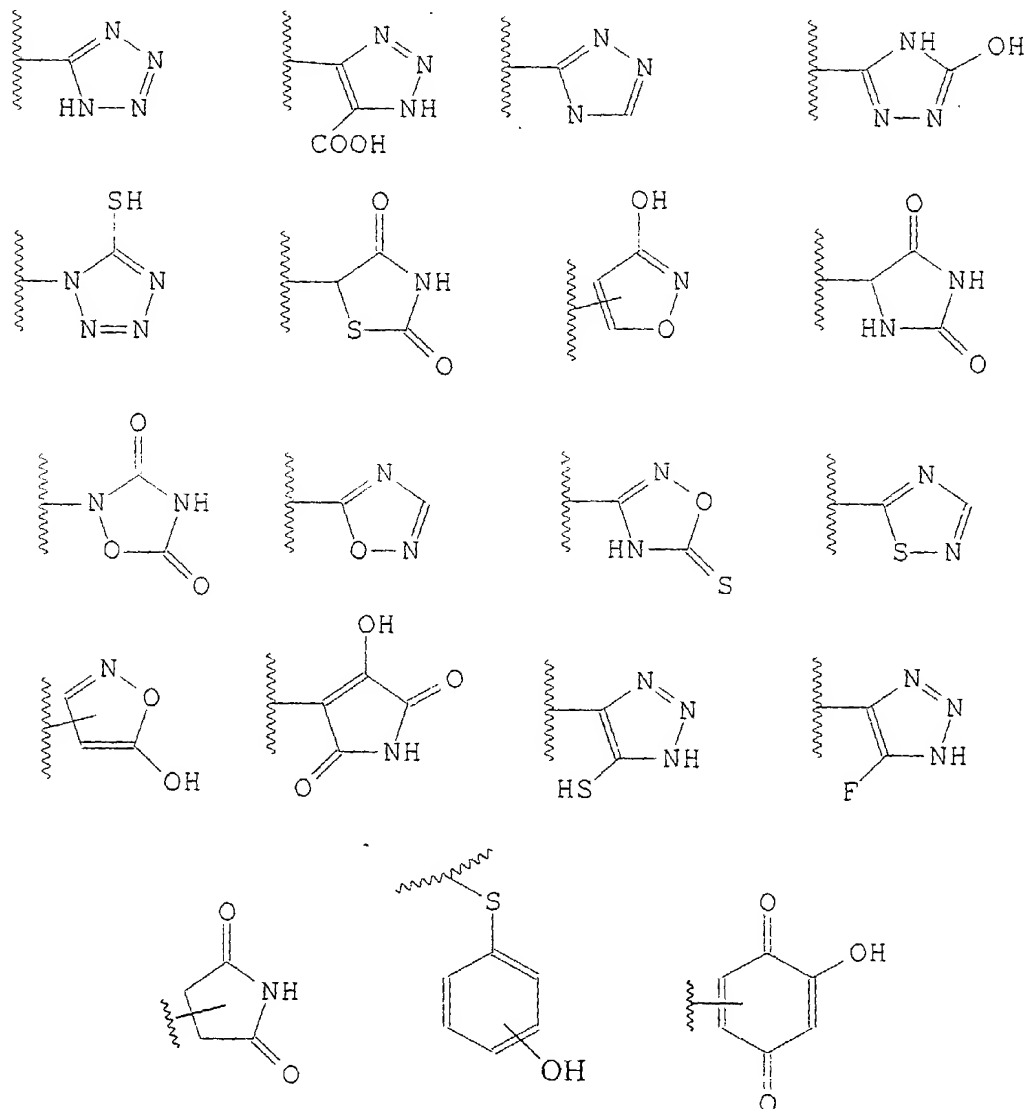
10. The pharmaceutical composition of claim 9, wherein R<sub>2</sub> is



a carbocycle or heterocycle containing any combination of  $\text{CH}_2$ , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with  $\text{R}^3$ .

5

11. The pharmaceutical composition of claim 9, wherein  $\text{R}_2$  is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with R<sup>3</sup>.

12. The pharmaceutical composition of claim 9, wherein R<sub>2</sub> is  
5 selected from the group consisting of:

-COOH; -SO<sub>3</sub>H,; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>;  
-NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>;  
-COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN..

10 13. The pharmaceutical composition of claim 9, wherein the  
N-heterocyclic carboxylic acid or carboxylic acid isostere  
compound is selected from the group consisting of compounds  
1-139.

15 14. The pharmaceutical composition of claim 8, further  
comprising a neurotrophic factor different from formula (I).

15. The pharmaceutical composition of claim 14, wherein said  
neurotrophic factor different from formula (I) is selected  
20 from neurotrophic growth factor, brain derived growth factor,  
glial derived growth factor, ciliary neurotrophic factor,  
insulin growth factor and active truncated derivatives  
thereof, acidic fibroblast growth factor, basic fibroblast  
growth factor, platelet-derived growth factors, neurotrophin-3  
25 and neurotrophin 4/5.

16. A method of treating a neurological disorder in an  
animal, comprising:

administering to the animal an effective amount of an  
30 N-heterocyclic carboxylic acid or carboxylic acid isostere  
to stimulate growth of damaged peripheral nerves or to  
promote neuronal regeneration.

17. The method of claim 16, wherein the neurological  
35 disorder is selected from the group consisting of peripheral

neuropathies cause by physical injury or disease state, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, and neurological disorders relating to neurodegeneration.

5

18. The method of claim 16, wherein the neurological disorder is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, amyotrophic lateral sclerosis, and Huntington's Disease.

10

19. The method of claim 16, wherein the neurological disorder is Alzheimer's disease.

15

20. The method of claim 16, wherein the neurological disorder is Parkinson's disease.

21. The method of claim 16, wherein the neurological disorder is amyotrophic lateral sclerosis.

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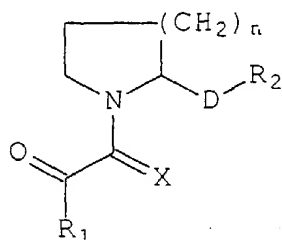
22. The method of claim 16, wherein the neurological disorder is Huntington's disease.

25

23. The method of claim 16, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

30

24. The method of claim 16, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



I

where

n is 1-3;

X is either O or S;

5 R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

10 R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere; and

-- wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

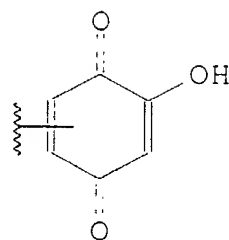
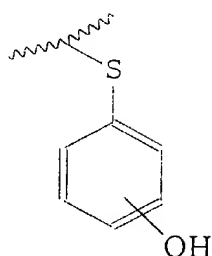
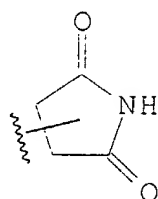
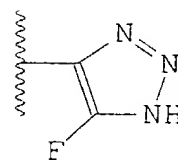
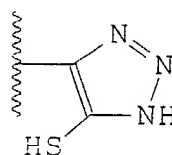
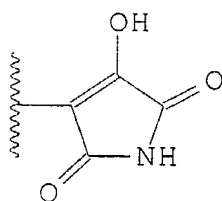
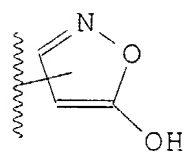
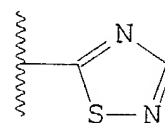
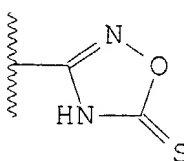
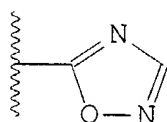
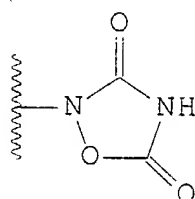
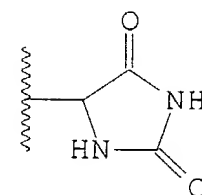
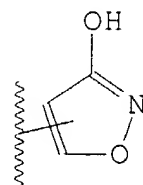
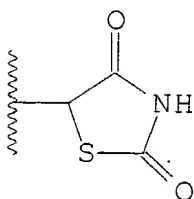
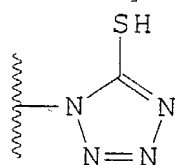
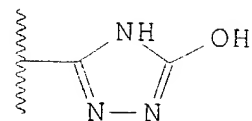
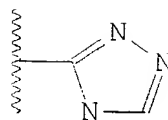
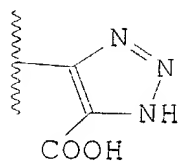
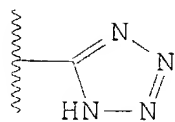
15 R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, 20 aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> where R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl;

or a pharmaceutically acceptable salt, ester, or solvate thereof.

25

25. The method of claim 24, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in 30 one or more positions with R<sup>3</sup>.

26. The method of claim 24, wherein R<sub>2</sub> is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

27. The method of claim 24, wherein  $R_2$  is selected from the group consisting of:

-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>; -NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>; -COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

28. The method of claim 16, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

29. The method of claim 16, further comprising administering a neurotrophic factor different from formula (I).

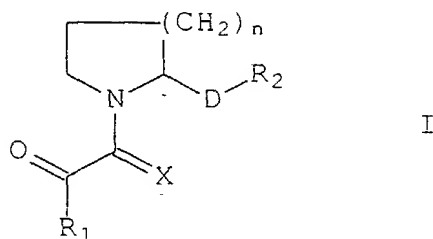
30. The method of claim 29, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

31. A method of stimulating growth of damaged peripheral nerves, comprising:

administering to damaged peripheral nerves an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere to stimulate or promote growth of the damaged peripheral nerves.

32. The method of claim 31, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

33. The method of claim 31, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):

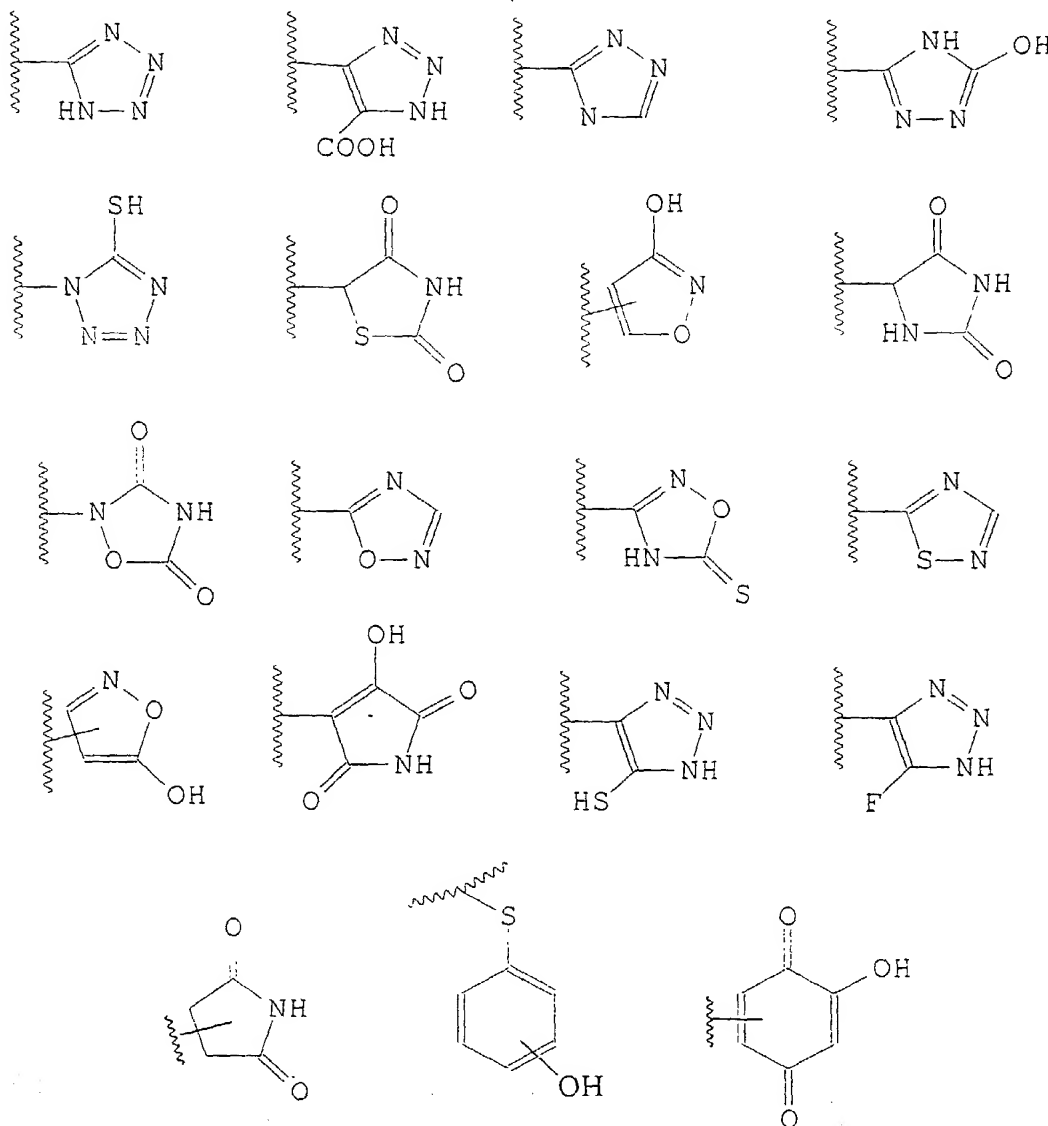


5 where  
 n is 1-3;  
 X is either O or S;  
 R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or  
 10 branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;  
 D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;  
 R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere;  
 15 and  
 wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R<sup>3</sup>, where  
 R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano,  
 20 nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> where  
 25 R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl;  
 or a pharmaceutically acceptable salt, ester, or solvate

thereof.

34. The method of claim 33, wherein  $R_2$  is a carbocycle or heterocycle containing any combination of  $CH_2$ , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with  $R^3$ .

35. The method of claim 33, wherein  $R_2$  is selected from the following group:





where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

36. The method of claim 33, wherein  $R_2$  is selected from the group consisting of:

-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>; -NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>; -COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

37. The method of claim 31, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

38. The method of claim 31, further comprising administering a neurotrophic factor different from formula (I).

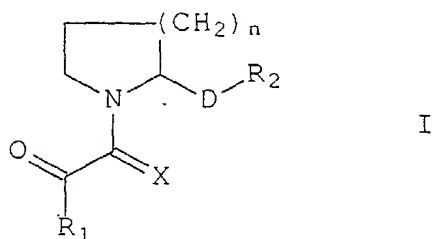
39. The method of claim 38, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

40. A method for promoting neuronal regeneration and growth in animals, comprising:

administering to an animal an effective amount of a N-heterocyclic carboxylic acid or carboxylic acid isostere to promote neuronal regeneration.

41. The method of claim 40, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

42. The method of claim 40, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):



5 where

n is 1-3;

X is either O or S;

10 R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere;

15 and

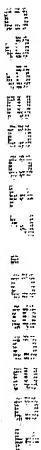
wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

20 R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> where

25 R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl;  
or a pharmaceutically acceptable salt, ester, or solvate

43. The method of claim 42, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with R<sup>3</sup>.

10



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

5 45. The method of claim 42, wherein  $R_2$  is selected from the group consisting of:

-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>; -NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>; -COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

10 46. The method of claim 40, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

15 47. The method of claim 40, further comprising administering a neurotrophic factor different from formula (I).

20 48. The method of claim 47, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

25 49. A method for preventing neurodegeneration in an animal, comprising:

30 administering to an animal an effective amount of a N-heterocyclic carboxylic acid or carboxylic acid isostere to prevent neurodegeneration.

50. The method of claim 49, wherein the neurodegeneration is Alzheimer's disease.

35 51. The method of claim 49, wherein the neurodegeneration

is Parkinson's disease.

52. The method of claim 49, wherein the neurodegeneration is amyotrophic lateral sclerosis.

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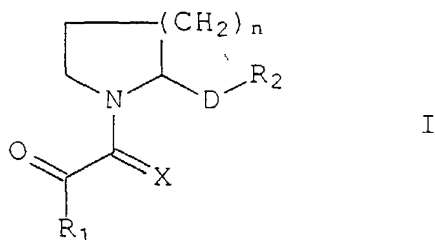
53. The method of claim 49, wherein the neurodegeneration is Huntington's Disease.

54. The method of claim 49, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

10

55. The method of claim 49, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises a compound of formula (I):

15



where

n is 1-3;

X is either O or S;

20 R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

25 D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere;

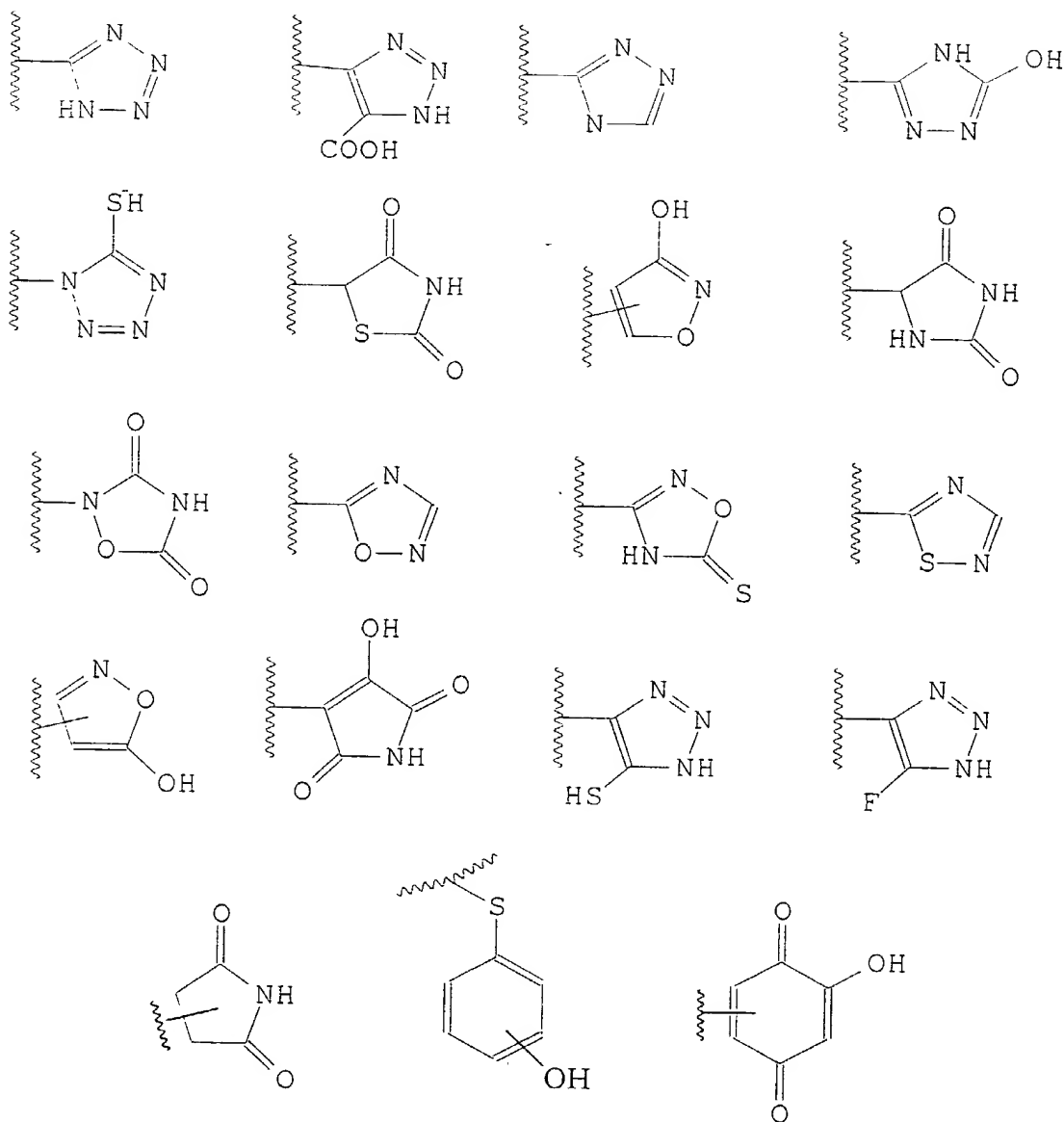
and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from  $R^3$ , where

5  $R^3$  is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl,  $C_1$ - $C_6$  straight or branched chain alkyl,  $C_2$ - $C_6$  straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and  $CO_2R^7$  where  
10  $R^7$  is hydrogen or  $C_1$ - $C_9$  straight or branched chain alkyl or  $C_2$ - $C_9$  straight or branched chain alkenyl;  
-- or a pharmaceutically acceptable salt, ester, or solvate thereof.

15 56. The method of claim 55, wherein  $R_2$  is a carbocycle or heterocycle containing any combination of  $CH_2$ , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with  $R^3$ .

20 57. The method of claim 55, wherein  $R_2$  is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with R<sup>3</sup>.

58. The method of claim 55, wherein R<sub>2</sub> is selected from the group consisting of:

-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>; -NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>; -COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

59. The method of claim 49, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere compound is selected from the group consisting of compounds 1-139.

60. The method of claim 49, further comprising administering a neurotrophic factor different from formula (I).

61. The method of claim 60, wherein said neurotrophic factor different from formula (I) is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor and active truncated derivatives thereof, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factors, neurotrophin-3, and neurotrophin 4/5.

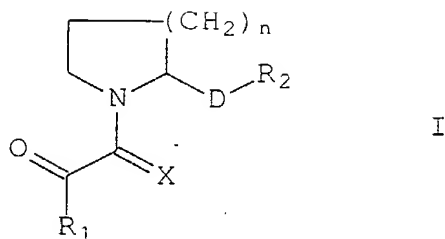
62. A method for treating alopecia or promoting hair growth in an animal, which comprises administering to said animal an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere.

63. The method of claim 62, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

64. The method of claim 62, wherein the N-heterocyclic



carboxylic acid or carboxylic acid isostere is a compound of formula (I):



where

n is 1-3;

X is either O or S;

R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere; and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sup>3</sup>, where

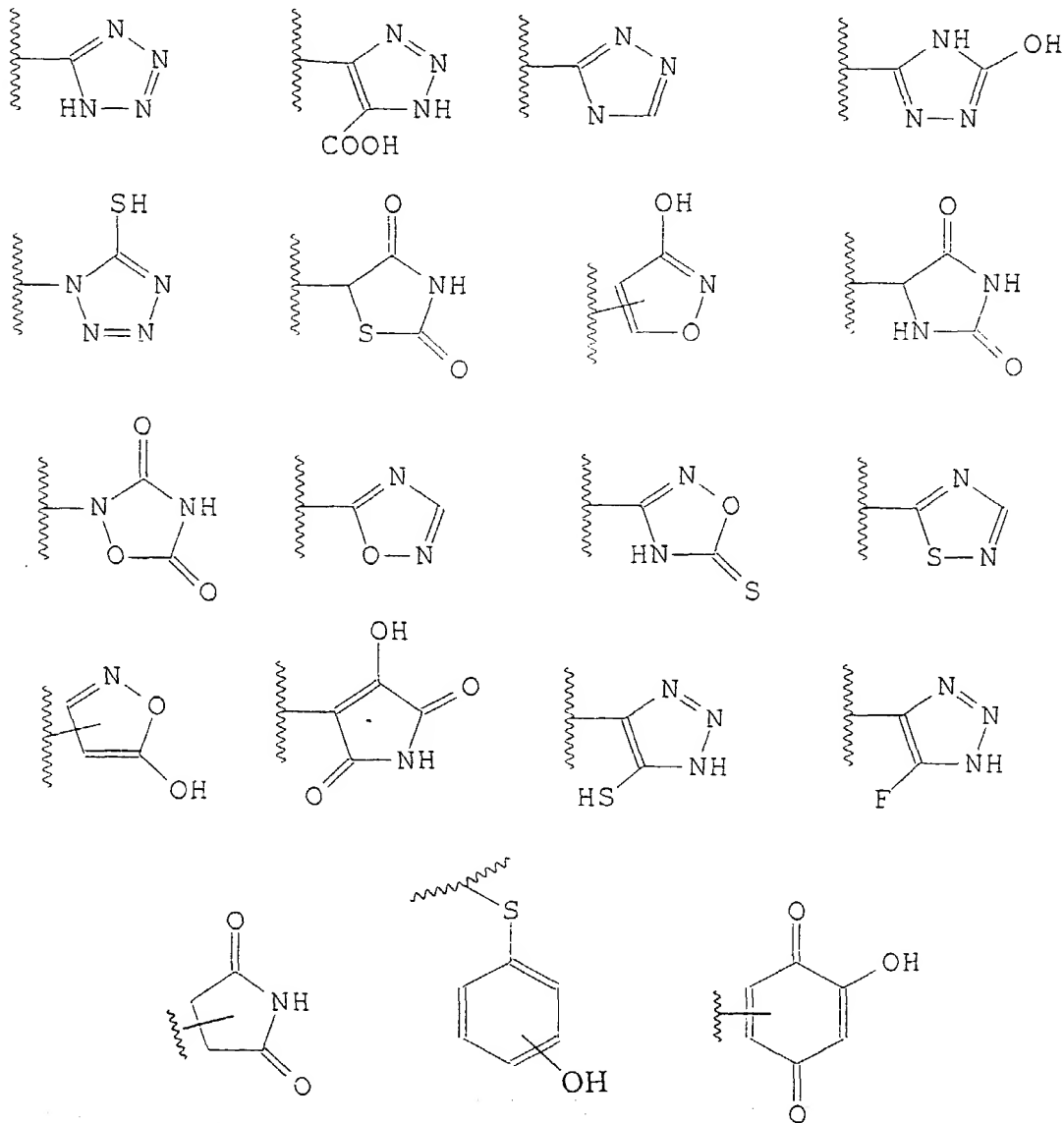
R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> where

R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl; or a pharmaceutically acceptable salt, ester, or solvate

thereof.

65. The method of claim 64, wherein  $R_2$  is a carbocycle or heterocycle containing any combination of  $CH_2$ , O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are optionally substituted in one or more positions with  $R^3$ .

66. The method of claim 64, wherein  $R_2$  is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

5 67. The method of claim 64, wherein  $R_2$  is selected from the group consisting of

-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>; -NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>; -COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

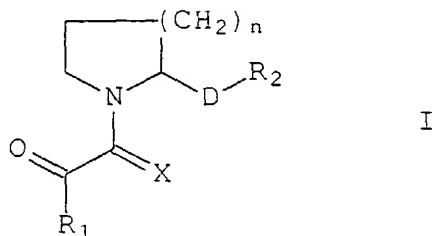
10 68. The method of claim 62, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-139.

69. A pharmaceutical composition comprising:

- 15 (i) an effective amount of a N-heterocyclic carboxylic acid or carboxylic acid isostere for treating alopecia or promoting hair growth in an animal; and
- (ii) a pharmaceutically acceptable carrier.
- 20

70. The pharmaceutical composition of claim 69, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

25 71. The composition of claim 69, wherein the carboxylic acid or carboxylic acid isostere is a compound of formula (I):



where

n is 1-3;

X is either O or S;

5 R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

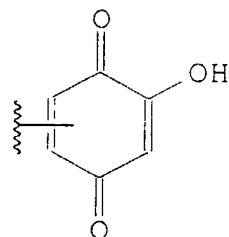
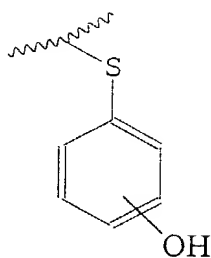
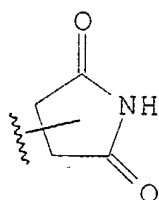
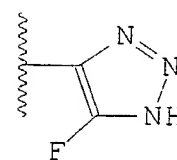
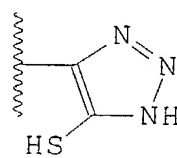
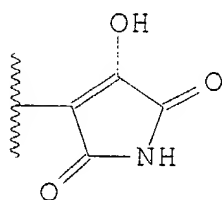
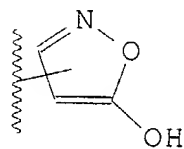
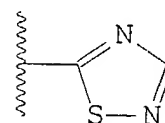
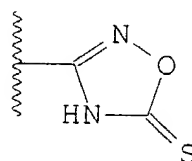
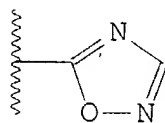
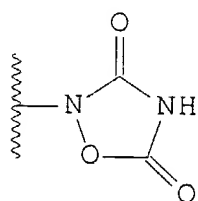
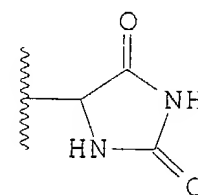
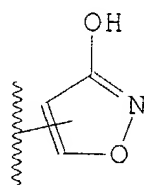
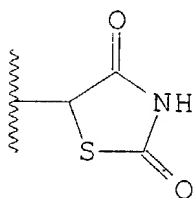
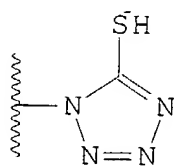
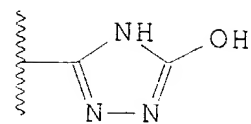
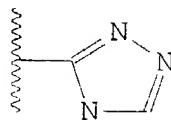
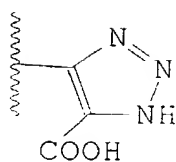
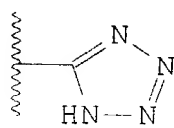
10 R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere; and

wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected  
15 from R<sup>3</sup>, where

R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> where  
20 R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl; or a pharmaceutically acceptable salt, ester, or solvate thereof.  
25

72. The composition of claim 71, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the  
30 atoms of said ring structure are optionally substituted in one or more positions with R<sup>3</sup>.

73. The composition of claim 71, wherein R<sub>2</sub> is selected from the following group:



where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

74. The composition of claim 71, wherein  $R_2$  is selected from the group consisting of:

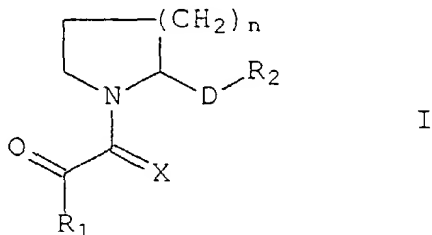
-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>; -NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>; -COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

75. The composition of claim 69, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-139.

76. A method for treating a vision disorder, improving vision, treating memory impairment, or enhancing memory performance in an animal, which comprises administering to said animal an effective amount of an N-heterocyclic carboxylic acid or carboxylic acid isostere.

77. The method of claim 76, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is non-immunosuppressive.

78. The method of claim 76, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere is a compound of formula (I):



where

n is 1-3;

X is either O or S;

5 R<sub>1</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, or a C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

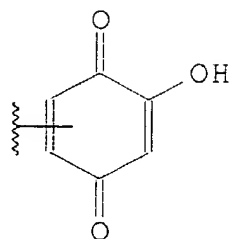
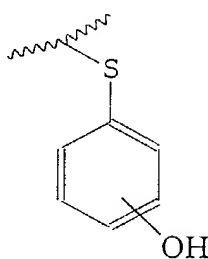
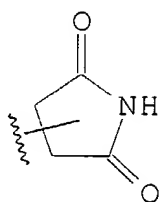
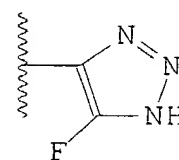
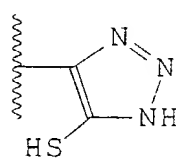
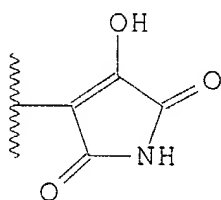
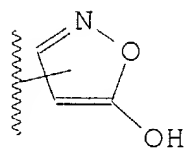
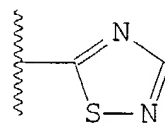
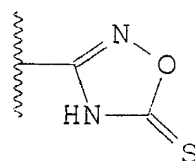
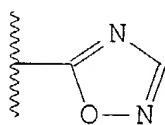
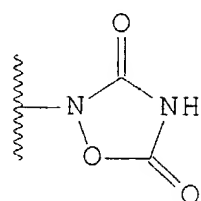
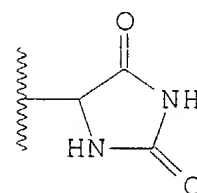
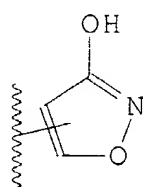
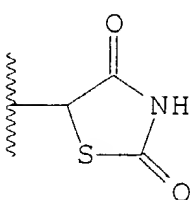
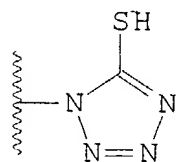
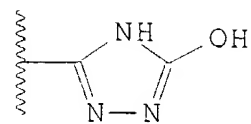
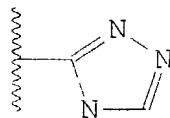
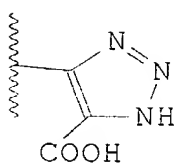
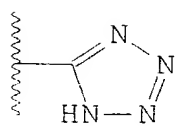
10 R<sub>2</sub> is carboxylic acid or a carboxylic acid isostere; and

-- wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected  
15 from R<sup>3</sup>, where

R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl,  
20 C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> where R<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl;  
or a pharmaceutically acceptable salt, ester, or solvate  
25 thereof.

79. The method of claim 78, wherein R<sub>2</sub> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the  
30 atoms of said ring structure are optionally substituted in one or more positions with R<sup>3</sup>.

80. The method of claim 78, wherein R<sub>2</sub> is selected from the following group:





where the atoms of said ring structure may be optionally substituted at one or more positions with  $R^3$ .

5 81. The method of claim 78, wherein  $R_2$  is selected from the group consisting of  
-COOH; -SO<sub>3</sub>H; -SO<sub>2</sub>HNR<sup>3</sup>; -PO<sub>2</sub>(R<sup>3</sup>)<sub>2</sub>; -CN; -PO<sub>3</sub>(R<sup>3</sup>)<sub>2</sub>; -OR<sup>3</sup>; -SR<sup>3</sup>;  
-NHCOR<sup>3</sup>; -N(R<sup>3</sup>)<sub>2</sub>; -CON(R<sup>3</sup>)<sub>2</sub>; -CONH(O)R<sup>3</sup>; -CONHNHSO<sub>2</sub>R<sup>3</sup>;  
-COHNSO<sub>2</sub>R<sup>3</sup>; and -CONR<sup>3</sup>CN.

10 82. The method of claim 76, wherein the carboxylic acid or carboxylic acid isostere is selected from the group consisting of compounds 1-139.